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Pediatric Neuroimaging Ethics

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Neuroimaging has provided insight into numerous neurological disorders in children, such as epilepsy and cerebral palsy. Many clinicians and investigators believe that neuroimaging holds great promise, especially in the areas of behavioral and cognitive disorders. However, concerns about the risks of various neuroimaging modalities and the potential for misinterpretation of imaging results are mounting. Imaging evaluations also raise questions about stigmatization, allocation of resources, and confidentiality. Children are particularly vulnerable in this milieu and require special attention with regards to safety guidelines and modality adaptations. This article examines pediatric neuroimaging practice through an ethics lens. Most authors in the field of neuroethics focus on the future concerns of neuroimaging. In contrast, our paper examines ethical matters surrounding current clinical applications in the pediatric population. We first provide a brief overview of the neuroimaging technologies most commonly used in a pediatric clinical context and then discuss a variety of ethical issues arising from the use of these technologies.

Neuroimaging Technology Overview

Structural Neuroimaging

Presently, structural, anatomic neuroimaging is the most commonly employed modality in the clinic.[1] Through localizing anatomical abnormalities, structural neuroimaging studies have demonstrated disorder-specific findings in children with a wide range of developmental impairments prenatally and postnatally. In clinical practice, structural neuroimaging is indicated in children with a wide variety of congenital, metabolic, neoplastic, inflammatory, and traumatic conditions. Computed tomography (CT) and magnetic resonance imaging (MRI) are two of the major imaging modalities in this category. Blood, gray matter, white matter, and spinal fluid are distinguished by differences in attenuation of an X-ray beam (in CT) or by differences in their response to radiofrequency pulses (in MRI).[2]

The strengths of CT are its low cost, examination speed, ready accessibility, and easy use.[3] New CT scanners produce high-resolution images in a matter of minutes, allowing patients to undergo the procedure without the need for sedation. However, radiation exposure may be a significant concern, especially with repeated examinations.

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MRI is the most widely used imaging modality in clinical pediatrics.[4] The clinical community considers MRI safe because, after 20 years of use, the vast majority of scans have been performed without incident and because no radiation exposure is involved.[5] MR imaging provides high anatomical resolution, and multiplanar imaging capability, which is not possible with CT scans.[6] MRI is disadvantageous because imaging time is relatively long, the imaging itself is motion sensitive, the scanner noise is loud, and the environment within the apparatus is constrained.[7] As discussed further in the section regarding imaging risks, these circumstances may necessitate sedation in some children. In addition, any plates, screws, or metallic implants are contraindications for MRI use because they may give rise to tissue damage under the influence of the magnetic field or malfunction in the case of electrical implants.[8]

Functional Neuroimaging

Functional imaging is broadly defined as those techniques used to provide measures of brain activity.[9] Functional neuroimaging modalities assume that there is a link between increased local brain activity and/or increased regional cerebral blood flow, blood volume, blood oxygen content, and changes in tissue metabolite concentration.[10] Functional modalities are being used to map localized cognitive processing and to examine brain plasticity. Positron emission tomography (PET), single photon emission computed tomography (SPECT), and functional MRI (fMRI) are examples of functional neuroimaging technologies.

PET is based on the detection of photons arising from the decay of injected radiotracer (i.e., radiolabeled molecules).[11] With the ability to image various radiotracers and their distribution within the brain, it is possible to follow molecular interactions and pathways.[12] Compared with CT and MRI, PET scanning offers the advantage of assessment of physiological and pathophysiological processes and can measure chemical changes that occur before visible signs of disease are present on CT and MRI images.[13] However, PET has several disadvantages, such as exposure to radiation (the dosage is comparable to CT), the substantial expense of the technology compared to other types of imaging, limited availability, and the need for bladder catheterization and sedation in some pediatric patients (though not routinely).[14] SPECT is similar to PET but is more readily available and considerably less expensive.[15] This modality measures changes in blood flow and receptor activity using different radiotracers while the data are used to create images of slices of brain on different planes.[16]

fMRI is a technique based on MRI that detects small fluctuations in the magnetic signal resulting from changes in blood oxygen level associated with brain activation.[17] The most frequently used technique is known as “blood oxygenation level dependent” (BOLD) contrast, which exploits tiny magnetization differences between oxygenated and deoxygenated blood (brain activation is followed by an increase in the ratio of oxygenated to deoxygenated blood).[18] Thus, fMRI measures blood flow and is an indirect measure of brain activity.[19] Although fMRI is considered noninvasive and as safe as MRI with the potential to provide insights into brain regions and networks associated with behavioral, cognitive, and other neurological disorders, this modality has several disadvantages in addition to those associated with MRI. For example, the coupling of brain activity to BOLD signal is assumed to be constant across different populations. Yet, aging, oxidative stress, and other factors may change this relationship.[20] Therefore, interpretation of images may be compromised. Furthermore, image analysis techniques need to be improved for pediatric populations[21] as fMRI is very sensitive to motion (more so than conventional MRI) and movement during scanning produces artifacts for which adjustments need to be made.[22] For example, although motion correction algorithms are recommended, and often effective, they are not entirely satisfactory, and in some circumstances may generate false signal assessments.[23]

Ethical Issues in the Pediatric Clinical Context

Risk Reduction and Description

In the pediatric clinical context, there are two very important risk-related ethical imperatives—to reduce risk where possible and to describe risks as accurately and completely as possible to those with the authority to provide consent to neuroimaging (most commonly the parents). Some specific risks are associated only with a specific neuroimaging modality, whereas unexpected findings, lack of child-appropriate protocols and equipment, and potential overuse of imaging technologies are problems common to all of the technologies. These risks have implications for clinical practice. In this section, we explore some of the risks of each technology and then some of the risks common to all of the technologies through the lens of risk reduction and/or risk description. The risks discussed are those on which we believe the ethical imperatives mentioned above would require action (Table 1).

MRI.

Direct physical risk: MRI scanners use a strong static magnetic field, a pulsed gradient magnetic field, and a radiofrequency field to obtain images of the body in selected planes.[24] Another component of MRI is the strong static magnetic field that is always present even when the scanner is not imaging.[25] Due to the intrinsic properties of the MRI scanner and its environment, patients are vulnerable to physical injury (see Table 1).

Detailed patient screening guidelines have been developed for the MR environment (www.MRIsafety.com). These guidelines help to reduce the risk of such harms as are encountered when a patient with a metal implant undergoes an MRI. Unfortunately, these guidelines do not specifically address pediatric concerns. Therefore, screening guidelines specific to children should be developed and disseminated.

According to Shellock and Crues,[26] most of the reported cases of MR-related injuries and the few fatalities that have occurred have been the result of failure to follow safety guidelines or the use of outdated information regarding the safety aspects of biomedical implants. For example, undetected or misplaced metal objects have caused injuries during MRI.[27] Therefore, guidelines should be better disseminated and compliance enforced. Furthermore, systemwide strategies to decrease the incidence of serious errors should be adopted—for example, the use of metal detectors over the doors of MRI examination rooms.[28]

Table 1. Risk Description

	MRI	CT	PET/SPECT
Direct physical risk	• Known and unknown risks due to high-strength, pulsed, and radiofrequency fields • Risks due to metal objects in MRI environment (“missile effect”) • Risks due to electronic or magnetic implantable devices	• Negative effects of X-ray radiation	• Radiation hazard
Indirect physical risk	• Risks due to side effects of sedation • Heating injury due to monitoring equipment • Risks due to side effects of gadolinium-based contrast agents		• Risks due to intravenous injection of radiotracer • Risks due to bladder catheterization
Direct psychological risk	• Fear, distress and potentially long-term psychological effects (i.e., claustrophobia) due to MRI environment and procedure		
Common risks • Ambiguous interpretation of clinical imaging results • Risk of unexpected findings • Potential risks due to lack of child-appropriate neuroimaging guidelines • Risks due to overuse of neuroimaging technologies			

Further research into risks associated with MRI is also necessary. Only a few epidemiological studies into MR exposure have been carried out; consequently, there is an insufficient scientific basis for the assumption that MR exposure has no long-term effects.[29] More research will provide a more solid foundation for claims about risks made during the consent process for MRI.

Indirect physical risk: The risks of MRI may not be directly related to the properties of the MRI magnet and environment. For example, under certain clinical circumstances, an MRI exam may require the administration of sedation or a contrast agent. These procedures introduce risk due to potential serious side effects.

The absence of patient motion is necessary for optimal MRI. Sedation has frequently been used to eliminate motion in children. Indeed, historically, sedation has been required in almost half of the pediatric patients who are imaged.[30] Unfortunately, pediatric sedation can have harmful effects. The risks of sedation, depending on the drug used, commonly include drowsiness, confusion, impaired judgment, nausea, and vomiting.[31] Rarely, complications may include difficulty breathing, brain damage, and death.[32] Alternatives to sedation in children are being, and should continue to be, explored: for example, the use of video/audio programs, late night scanning, patient preparation using simulation techniques, and increased speed of imaging time.[33] In addition, technological problems are associated with monitoring sedated patients in a MR imaging scanner. For example, electrocardiogram monitoring during MR imaging has been associated with heating or burning injuries and should be used with caution in this setting.[34]

Additional guidelines are also needed. Guidelines have been developed by the American Academy of Pediatrics in its *Monitoring and Management of Pediatric Patients During and After Sedation for Diagnostic and Therapeutic Procedures*. However, disabled children may have unpredictable responses to sedation.[35] Therefore, clear sedation guidelines need to be developed for the disabled pediatric population.

MRI delivery guidelines are also needed. For example, consider the use of gandolinium in a pediatric population. Gandolinium is a commonly used MRI contrast agent. It has a slower clearance in fetuses, neonates, and infants compared to adults.[36] Reported adverse effects include thrombophlebitis, hypotension, headache, nausea, and vomiting.[37] Due to these possible adverse events, clear guidelines should be developed around the use (or possible elimination) of gandolinium and other contrast agents in MRI procedures in children.

Direct psychological risk: The MRI procedure may produce considerable fear, distress, and potentially long-term psychological effects for a significant proportion of patients.[38] Anxiety, fear, and stress due to claustrophobia in MRI devices need to be taken into consideration in the clinic. Many children become anxious during scanning and may become uncooperative.[39] Familiarity and comfort with the people acquiring the scan or bringing in a favorite blanket or stuffed toy are some methods by which to make MRI more pleasant for the child.[40] The staff of the MRI center must be flexible and willing to make a commitment to the additional resources needed to tailor the procedures to the individual child.[41] The findings from the studies just mentioned should be considered by all facilities offering pediatric MRI, and standard operating procedures based upon them should be developed and implemented.

CT. A significant risk associated with CT scanning is the negative effect of X-ray radiation. This risk is generally considered quite small compared to the benefits of accurate diagnosis and treatment. However, one report has suggested that CT scans of children are often done without adjusting dose to weight, resulting in up to 50% of the dose being unnecessary.[42] Furthermore, children are generally at a higher risk of long-term adverse health effects due to imaging radiation exposure because of their greater life expectancy.[43] The lowest radiation dose necessary for an accurate diagnosis should be used.[44] Significant dose reductions, especially in children, can be achieved without compromising clinical efficacy.[45] Picano[46] suggests that clinicians are not sufficiently aware of the possible long-term health risks associated with radiological imaging. Clear guidelines need to be set for all levels of clinical applications of CT scanning.

PET/SPECT. The radiation hazard posed by PET is said to be low and equivalent to the hazard posed by CT scan[47] as the radioisotopes administered do not stay in the body for long due to their short half-lives. However, radiation dose level from intravenous injection of PET radiotracer in infants has been reported in only one study.[48] More research is therefore needed to determine the actual risk of PET in children. This need for research is even greater for SPECT as, compared to PET, SPECT uses lower energy isotopes that have longer half-lives and as SPECT is frequently used in the clinic due to its relative simplicity and lower costs.[49]

In addition, PET and SPECT imaging often require intravenous administration of radiotracers. PET/SPECT technologists do not always have experience establishing intravenous access in children.[50] This procedure may be particularly challenging and distressing for children, and, therefore, close attention should be paid to the training of personnel to ensure that they have adequate skills in establishing pediatric intravenous access. Bladder catheterization should be performed by experienced technologists with pediatric neuroimaging expertise.[51]

Risks common to various technologies. Both magnetic and radiological imaging share additional risks that may be of particular concern in the pediatric population. Special precautions need to be taken when reading the brain images of children to ensure detection of any anomalies as well as appropriate follow-up.[52] In particular, concerns have arisen regarding functional imaging for which findings are frequently equivocal in terms of clinical significance.[53] Having an experienced radiologist, as opposed to a nonspecialist physician, involved in the review of neuroimages or readily available for referral is essential to the well-being of neuroimaging patients.

Reports of unexpected MRI findings in brain imaging are not uncommon in the clinical domain and have been reported in pediatric populations.[54] These reports compel consideration of the ethical issues of disclosure of risk of unexpected findings in the consent process as well as the appropriate responses to unexpected findings (e.g., what parents should be told about the possibility of unexpected findings during the consent process, who should be involved in the evaluation of the findings, and who should be told of these findings). Guidelines need to be created around the procedures to be followed to deal with the prospect and realization of unexpected findings.[55]

There have been many complaints in the literature that child-appropriate neuroimaging protocols have not been developed. These types of protocols would ensure that pediatric subjects comprehend the procedure and experience a minimum of fear.[56] Such protocols would also ensure imaging environment adaptations and modifications to improve data acquisition and accuracy in the neuroimaging of children. For example, the reduction of scan time for children ought to be prioritized, and video/audio presentation devices and technologies that minimize motion difficulties ought to be readily available to the imaging team.[57] Even the technology needs to be improved, as, for example, allowing easy placement of devices in newborn intensive care units and minimizing imaging time will allow for safer and more accurate acquisition of information.[58]

Another risk common to neuroimaging technologies is the potential overuse. Up to a third of all radiological examinations have been reported as totally or partially inappropriate.[59] Again, radiologists have an important role in protecting children from unnecessary exposure to radiation and the risks associated with neuroimaging by curtailing their overuse.[60]

Interpretation

Several articles have warned of the potential for misinterpretation or overinterpretation of imaging examination results.[61] The reasons for this potential misinterpretation are related to the technological infancy of most neuroimaging modalities, the rapid evolution of the technology, lack of standardization, and methodological inconsistencies.

The limits of interpretative powers. Conventional MRI and CT image interpretation requires knowledge of normal brain anatomy and development, recognition of findings in specific disorders, and an awareness of potential study artifacts. Although neuroanatomical imaging measures the volume and shape of brain structures, the underlying cause of any differences may not be determinable.[62] Regarding neurobehavioral disorders, most imaging studies of learning disabled patients using MRI or CT have not identified significant structural pathology.[63] Additionally, many neurological disorders are the result of complex interactions between many factors, and causality may not be clearly established.

Functional neuroimaging has encountered criticisms based on the interpretation of functional–behavioral associations and the lack of standardization in the field. For example, functional neuroimaging cannot determine that a particular cognitive process causes imaged brain activity because this association has not been proven to be causal.[64]

Additionally, the structure and content of neuroimaging data sets currently have no universally accepted standards.[65] Data formats, statistical analyses, behavioral descriptors, and choice of controls (or baseline conditions) are poorly defined and variable across different laboratories. This makes accurate interpretation of research results difficult and, in turn, affects the accuracy of clinical results.[66]

The interpretation of neuroimaging examination results faces further challenges when children are imaged. Because the developing brain is constantly changing, a certain degree of normal variability must be taken into consideration when interpreting pediatric neuroimaging data.[67] Brain structure varies during childhood as do activation patterns in cognitive strategies measured in functional imaging.[68] Additionally, a number of neurological parameters in children differ from those observable in adults and yet, for the pediatric population, limited neuroimaging research data exist.[69] For example, developmentally accurate child brain maps are not yet freely available, resulting in the use of adult brain maps for analysis that may lead to incorrect identification of brain regions in children.[70] For various ethical and practical reasons, extensive neuroimaging studies with control groups (i.e., healthy children) have not been carried out. However, many authors have called for improved and increased research into pediatric neuroimaging in order to address questions surrounding data analysis.[71]

Neuroimaging is still at a relatively early stage of development. Although it has allowed researchers and clinicians to view the human brain more thoroughly than ever before, the comprehensive analysis, interpretation, and standardization of imaging data are daunting tasks.

The ethical implications. The present technological and interpretive limitations directly influence the ethical aspects of neuroimaging in the clinic. Although some structural changes (e.g., discrete tumors or lesions) can be unambiguously identified via neuroimaging, other structural abnormalities can be much more subtle.[72] Neuroimaging is recommended by the American Academy of Neurology (AAN) as part of the diagnostic evaluation of the child with cerebral palsy and global developmental delay, to determine neurodevelopmental outcome in encephalopathic term infants, and to evaluate the first nonfebrile seizure in children. According to the AAN, whether MRI, CT, or other imaging techniques are used depends on the disorder, the age of the patient, and specific clinical circumstances. Comprehensive, as opposed to piecemeal, instruction regarding the clinical utility and accuracy of pediatric neuroimaging is needed to aid in diagnosis and prognosis and to give clinical confidence.[73]

Functional imaging is very important for presurgical planning—especially in epilepsy surgery—and has the potential to provide insight into neurological and psychiatric disorders.[74] However, in some cases, due to insufficient scientific evidence, the use of functional imaging in the diagnosis of developmental and behavioral disorders is not advocated. For example, the Practice Guideline of the American Academy of Pediatrics in its *Diagnosis and Evaluation of the Child with ADHD* does not recommend diagnostic neuroimaging in ADHD patients. Moreover, the American Academy of Neurology does not advise the use of functional modalities, such as SPECT, in the clinical diagnosis of autism. Problems arise in the setting of standards because of the variability of reported diagnostic accuracy, imaging techniques, timing of the imaging examination, and variations in maturation of the developing brain.[75] Given the plasticity of pediatric neurodevelopment, the analysis of the images of children should merit special attention at the level of the clinic. A healthy degree of humility and realism supports admitting diagnostic and prognostic limitations while upholding high standards for diagnostic and predictive accuracy.

Stigmatization

A noticeable feature of some neuroimaging studies is the use of value-laden language to describe various aspects of brain structure and function even though normal brain anatomy and function has yet to be determined. The language implies the existence of normal and abnormal brain templates and increases the potential for the stigmatization of pathologically labeled individuals. Special precautions will need to be taken in this regard in respect of cognitive profiling, intelligence tests, and behavioral disorders diagnosis. Despite this, Giedd[76] has noted "the growing use of SPECT scans to diagnose and guide treatment for disorders such as ADHD and juvenile-onset bipolar disorder." This trend is occurring notwithstanding discouragement from relevant professional organizations such as the American Academy of Pediatrics and the American Academy of Neurology[77] regarding the use of neuroimaging to diagnose behavioral disorders. The behavioral and cognitive categorization of children using ambiguous labels, and the broad diagnostic criteria presently available raise serious ethical concerns.

Research on children's mental disorders has lagged behind parallel efforts for adults.[78] In addition, despite considerable progress in recent decades, the validity of many forms of child and adolescent diagnostic modalities is far from fully established.[79] Although accurate diagnosis could reassure family members and provide important information about prognosis, indiscriminate labeling, especially in the area of behavioral or mental disorders, could be harmful.[80] For example, early childhood neuroimages may lead to the unnecessary labeling of a child as developmentally delayed while not taking into consideration brain plasticity and the potential resilience of children.[81] Individuals could be seen as hardwired for behavioral problems, chronically ill, and unable to change or adapt. Using brain imaging to predict emotional and mental outcomes may stigmatize a child and affect how he or she is raised. The image diagnosis may influence clinical care as well as parental treatment and later educational decisions.[82] In addition, children diagnosed with behavioral and emotional disorders are highly likely to receive peer rejection.[83]

Allocation of Resources

Serious ethical issues also arise when examining neuroimaging and allocation of resources. At the societal level, pediatric neuroimaging raises several questions surrounding its potential exclusivity, expense, and the medicalization of social phenomena. For example, with the advent of private MRI clinics, imaging modalities may permit queue jumping so that any potential benefits will favor those with the resources to afford access. Additionally, the expense of neuroimaging may restrict access to wealthy communities and regions. This potential inequality needs to be acknowledged, and investigations into the best use of public funds for neuroimaging techniques should be undertaken. Another potential concern relates to the massive funds allowed for the development of neuroimaging modalities to the detriment of basic community-based and family services.[84] Although technologically based interventions are important for the study of brain development, the emphasis on neuroscience and neuroimaging data must be balanced with the environmental influences on health and disease.[85]

Neurobiological explanations may be viewed as more objective than environmental descriptions. However, environmental factors, although more complex and nuanced, may provide insight into the deeper social causes of particular neurological disorders. A focus on neuroimaging procedures could channel resources away from environmental concerns, such as the consequences of poverty on children. For instance, not only is prematurity more common in low-income populations, but the developmental outcomes for these infants born into poverty are significantly worse than for middle-class preterm infants.[86] Elaborate technological answers to neurobehavioral problems are not necessarily as immediately efficacious as basic public health responses.

Confidentiality

The importance of the privacy and confidentiality of children's health information has been recognized by several professional and international organizations.[87] Neuroimaging information itself could be considered sensitive information. For example, results from functional neuroimaging tests may be predictive in nature or may be diagnostic for behavioral, cognitive, or mental disorders. Furthermore, especially where results are equivocal, confidentiality must be maintained so that findings with unclear functional interpretation are not subject to misuse.[88] Although considerable attention has been paid to establishing practices directed at protecting patient privacy, still more work needs to be done. For example, there will be increasing interest in the possibility of data mining in banks of neuroimages. Thus, clinicians should consider anticipating future research uses and including a consent to be contacted in the future about research projects in the consent process for clinical neuroimaging.

Secondary information obtained in the process of patient screening also raises ethical concerns. Specifically with regards to MRI procedures, patients must be screened for such personal information as presence of IUDs, diaphragms, tattoos, and body piercings.[89] Two questions immediately arise. First, who should be given this secondary information? For example, can or should the parents be told about body piercings that they know nothing about? Second, how can inadvertent disclosure of this secondary information during the screening process be avoided? For example, if a pregnancy test is included in the screening process, how can the minor's privacy be protected if the parent has accompanied the minor to the screening?

Concern about confidentiality is one of the primary reasons young people delay seeking healthcare services for sensitive issues.[90] The protection of privacy in adolescent care has been justified from a developmental perspective based on adolescents' need for increasing autonomy as they approach adulthood and their increasing capacity to give informed consent.[91] The particular problems that may be of concern to the pediatric populations undergoing neuroimaging examinations mentioned above have not yet been thoroughly addressed. Clinics must develop clear confidentiality policies and privacy-protecting practices.[92]

Conclusion

Neuroimaging is a developing field that holds great promise in aiding diagnosis, prognosis, and treatment of pediatric neurological disorders. However, as outlined in this paper, many unknowns and numerous complex risks surround neuroimaging technologies. Children, especially disabled children, are particularly vulnerable groups that require special attention. Clinicians within the field of neuroimaging who work with the pediatric population ought to be aware of the particular needs of children. Additionally, clear guidelines and standards need to be developed around the use of neuroimaging technologies to provide diagnostic and prognostic accuracy and confidence. The creation of standards for a technology still in development could be a difficult task. However, given the fact that these technologies are presently being used in the clinic and perhaps imprudently, clinicians need guidance.

In our paper, we have highlighted the areas in need of further clarification and research, including:

1. Development of detailed guidelines with respect to pediatric neuroimaging, especially of disabled children.
2. Adaptation of neuroimaging modalities to accommodate the particularities of the pediatric population.
3. Clinician assurance that risks are accurately and completely disclosed to parents and mature minors.
4. Development of guidelines for assessing risk versus benefit (e.g., when pediatric neuroimaging is obligatory or optional).
5. Development of best practices for handling unanticipated findings.
6. Restraint in interpretation of results to mitigate inappropriate diagnoses and prognoses.
7. Advancement of research into the environmental (including psychosocial environment) influences on pediatric neurological disorders alongside the development of neuroimaging technologies.
8. Development of clear confidentiality policies and privacy protection practices for the children undergoing neuroimaging examinations.

Through the resolution of these issues, neuroimaging could better achieve its promise for the pediatric population. Safe and responsible use of neuroimaging technologies and analysis of neuroimages promote the best interests and well-being of the pediatric patient.

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